Evaluation of cardiac troponin dynamics as an early biomarker for anthracycline-induced cardiotoxicity

Published: 23-08-2024
Last updated: 21-12-2024

Identification of the dynamics of hs-cTnI and hs-TnT release during and after anthracycline treatment (doxorubicine in combination with cyclofosfamide) in breast cancer patients in order to determine the optimal sampling time point, most reflective...

Ethical review	Approved WMO
Status	Pending
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Observational non invasive

Summary

ID

NL-OMON56966

Source
ToetsingOnline

Brief title
ANTROP-study

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
cancer, oncology

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis
Source(s) of monetary or material Support: St Antonius onderzoeksfonds

Intervention

Keyword: anthracyclines, cardiotoxicity, troponins

Outcome measures

Primary outcome

Identification of the dynamics of hs-cTnI and hs-TnT release during and after anthracycline treatment (doxorubicine in combination with cyclofosfamide) in breast cancer patients in order to determine the optimal sampling time point, most reflective of the (total) cardiac damage.

Secondary outcome

Evaluation of the relation between summary parameters for troponin exposure (Cmax, relative increase of troponin from baseline and AUC) and cardiotoxicity, defined as persistent LVEF decline and/or development of symptomatic heart failure. (This endpoint is explorative)

Study description

Background summary

Anthracyclines are the cornerstone of adjuvant breast cancer treatment. However, anthracyclines are known to cause irreversible damage to cardiomyocytes. The cumulative lifetime dose of anthracyclines is an important predictor of development of heart failure. Regardless of administering doses below this maximum cumulative life time dose, approximately 20% of patients develop a persistent decrease in LVEF and about 5% develops symptomatic heart failure.
In order to attenuate the cardiotoxic effects of anthracyclines, cardiac imaging is performed in high risk patients (e.g. patients with pre-existent significant cardiovascular disease), including quantification of the LVEF at baseline and during or after treatment. This is a reactive monitoring strategy, since it does not detect early cardiac damage and identifies only advanced cardiac injury. Cardiac troponins are specific markers for myocyte damage. Previous studies have shown a relationship between troponin increment during

anthracycline treatment and cardiotoxicity. Measuring cardiac troponins is therefore a promising strategy for early detection of cardiac damage. Though current monitoring guidelines recommend sampling of cardiac troponins in high-risk patients at baseline and throughout treatment, a standardized approach for timing and interpretation of troponin levels is not available. Clinical implementation of troponin measurements in monitoring protocols has therefore been limited. The optimal timing and interpretation of the troponin values remains unknown.
In this pilot study we aim to identify the dynamics of hs-cTnI and hs-TnT release during and after anthracycline treatment (doxorubicine in combination with cyclofosfamide) in breast cancer patients in order to determine what time point is most reflective of the (total) cardiac damage.

Study objective

Identification of the dynamics of hs-cTnI and hs-TnT release during and after anthracycline treatment (doxorubicine in combination with cyclofosfamide) in breast cancer patients in order to determine the optimal sampling time point, most reflective of the (total) cardiac damage.

Study design

Prospective observational (pilot) study.

Study burden and risks

The patient has no direct benefit from participating in this study. The obtained data will be used to assess the dynamics of troponin during and after anthracycline treatment. Insight in these dynamics will contribute to using troponin as a routine biomarker for management of anthracycline-induced cardiotoxicity, by determining troponin sampling time point(s) and cut-off values for future patients. Patients included in the study will be treated according to standard local protocol with 4 cycles of doxorubicin and cyclofosfamide followed by 12 cycles of paclitaxel. In the local protocol 11 sampling time points are scheduled for periodic laboratory check. During these same time points an additional blood sample will be drawn (lithium heparin tube, 4 mL). There will be no additional venapunction and no additional visit. The additional patient burden by participation in this study is therefore considered minimal.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Female
- Age >= 18 years
- Patients that are to be treated for breast cancer in the adjuvant setting with one of the following treatment schedules, in accordance with SAZ protocols:
o Doxorubicine and cyclofosfamide q2w for 4 cycles, followed by paclitaxel q1w for 12 cycles
o Doxorubicine and cyclofosfamide q3w for 4 cycles, followed by paclitaxel q1w
- Informed consent form (ICF) signed prior to participation in the study.

Exclusion criteria

Patients that already started treatment in one of the above described protocols are not eligible for inclusion, since a baseline sample is necessary.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2024
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO

Date:	23-08-2024
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL86515.100.24